FTR

SB 418 - FAQ

By: Dr. Joseph B. Guarnaccia, MD and Marina A. Creed, RN, BSN

What is the proposed legislation?

SB 418 prevents health insurers from excluding coverage of 'off-label' prescription medications for covered conditions if the drug has been recognized in one of three standard medical reference compendia or **"in peer-reviewed medical literature generally recognized by the relevant medical community."**

Why is this law necessary?

SB 418 replaces the existing law, which is outdated because it references only the three compendia:

(1) The U.S. Pharmacopoeia Drug Information Guide for the Health Care Professional (USP DI);

(2) The American Medical Association's Drug Evaluations (AMA DE), and

(3)The American Society of Hospital Health-System Pharmacists' American Hospital Formulary Service Drug Information(AHFS-DI).

Of the three, only the AHFS-DI is still published. The USP-DI was last published in 2005 and the AMA-DE last published in 1986.

The proposed new legislation expands the criteria to include "peer-reviewed medical literature," which is defined in the bill.

What is an 'off-label' drug?

An FDA-approved drug is called 'off-label' when it is used to treat a medical condition for which it has not received a specific FDA 'indication' or 'label' for the drug, which is described in the drug's Package Insert. This indication or label is narrowly based on the results of clinical trials conducted by the pharmaceutical company to obtain such an indication. Once a drug is approved, however, a medical practitioner may prescribe it to treat other diseases as well. The FDA does prohibit pharmaceutical companies from advertising or otherwise promoting the drug to treat conditions not included in the label.

New uses for drugs may have been found, and often medical evidence supports the new use. But the makers of the drugs have not put them through the formal, lengthy, and often costly studies required by the FDA to officially approve the drug for new uses (FDA, 2014).

Have other states enacted similar legislation?

Yes, at least 19 states have laws requiring coverage for 'off-label' medications and the National Association of Insurance Commissioners approved a model act calling for coverage of such drugs under specified conditions. (AFSCME, 2015) Federally, Medicare and Medicaid currently provide reimbursement for 'off-label' prescription medications.

How common is 'off-label' drug prescribing?

'Off-label' drug prescribing is very common, particularly in life threatening diseases such as cancer, chronic diseases such as multiple sclerosis and other autoimmune diseases, and in special populations of patients such as children or the elderly, who typically are not subjects in clinical trials. 'Off-label' drug use is very common with estimates that up to 50 percent of prescriptions in selected medical conditions are 'off-label' for that condition.

Why would a physician prescribe a drug 'off-label'?

There may be limited options for patients with life threatening or chronic diseases. It is generally recognized that there may be different etiologies for what we categorize for a single disease definition. Therefore, trying drugs with different mechanisms of action may be necessary to find a particular treatment that helps a patient. As previously stated, a drug may be indicated to treat adults with the disease, but never tested in pediatric patients with the same particular condition, and, therefore, its use would be considered off label. Smaller studies may show that a particular drug works in another disease, but given business considerations, e.g., limited profitability because of patent expiration, the limited size of the potential market for the drug or competition from an existing product, a pharmaceutical company chooses not to pursue the development of that drug for a different purpose.

An 'off-label' drug may be an older, generic drug that over the course of time becomes part of general medical practice to treat a particular condition, i.e., many of the drugs to treat migraine headaches, for example.

Physicians accept a higher level of responsibility when prescribing off-label treatments and, therefore, have to have a degree of confidence that the treatments are not only effective, but safe. There may be a greater risk of a malpractice action if the treatments cause harm compared to the use of an indicated therapy. Physicians who prescribe an off label treatment tend to be well-informed, subspecialists in that particular condition. Physicians generally would, and should, prescribe on-label treatments whenever possible but there are a number of situations where patients have tried and failed to gain benefit from on-label treatments and require more complex medical care.

Is it safe to use a drug 'off-label'?

Good medical practice and the best interests of the patient require that physicians use legally available drugs, biologics and devices according to their best knowledge and judgement. If physicians use a product for an indication not in the approved labeling, they have the responsibility to be well informed about the product, to base its use on firm scientific rationale

and on sound medical evidence, and to maintain records of the product's use and effects. (FDA, 2015)

Why not rely on standard medical compendia?

As stated previously, two of the three compendia that the current state law references are no longer in print. Medical science is a dynamic field with trends in treatment reflecting cutting edge advances scientific research. Of course, the practitioner has to balance what is novel with a solid scientific foundation and experience in a particular specialty. But entries in compendia and even medical review articles may be written by physicians who do not have any particular experience in a disease state and tend to be overly conservative.

As one study published in the Annals of Internal Medicine in 2009 on 'off-label' drug use, concluded, "Oncologists relyon compendia for up-to-date access to evidence and reimbursement information for 'off-label' indications. Current compendia lack transparency, cite little current evidence and lack systematic methods to review or update evidence."

How do healthcare insurers establish criteria for treatments?

Health insurers publish drug 'formularies,' which list medications that may be used for specific conditions. Often these formularies rely on FDA-approved indications for a specific drug. The formularies, however, may exclude drugs with FDA-approved indications on the basis of redundancy or cost, among other possible reasons. 'Non-formulary' drugs, including labelled and 'off-label' treatments, may be approved after a written or verbal appeal by the prescribing physician in what is known as a 'peer to peer review.' Ideally, this process should result in a positive outcome for the patient. The treating physician discusses particulars of a patient's case and justifies the use of a non-formulary treatment, whether it is 'on-label' or 'off-label', and, if the justification is sufficient, the insurer's physician representative approves the treatment.

While some health care insurers adhere to the principles of the 'peer to peer review' process, others treat is a 'pro forma' exercise to uniformly deny 'non-formulary' treatments based on inflexible guidelines. This can result in adverse outcomes for the patient and significant time, effort and frustration on the part of the physician trying to provide the best possible care for his or her patient. Furthermore, the lack of uniformity in the peer review process may give some insurers an unfair advantage compared to their competitors.

Would a more permissive policy towards 'off-label' treatments drive up the cost of healthcare premiums and increase the cost of healthcare?

Chronic diseases cause significant human suffering and have tremendous direct and indirect costs to families and society in terms of lost income from unemployment, costs of medical care to treat complications of the disease, and the economic and personal burden of care on family

members. Any treatments that are effective in treating chronic conditions have significant cost savings.

Furthermore, studies have shown that 'off-label' treatments may, in a number of situations, be less expensive than 'on-label' treatments. The reasons for this are that 'off-label' treatments are generally older than 'on-label' treatments and are more likely to be generic versions of marketed drugs. Drug development, particularly for drugs that are novel to medical practice, is an expensive, time consuming and risky endeavor. Pharmaceutical companies are under pressure to pursue development of drugs which are most likely to produce significant profits. In fact, most of the new drugs that are approved 'on-label' are 'repurposed', often based on existing drugs used to treat other diseases or altered versions of existing 'on-label' products.

CASE STUDY – Use of Rituximab in Multiple Sclerosis

Rituximab is biological drug that has been on the market for many years and is approved to treat certain kinds of lymphoma and rheumatoid arthritis. Compared to existing approved drugs for multiple sclerosis, rituximab has a novel mechanism of action that is gaining significant credence in the medical scientific literature. There are several medical studies that support the use of rituximab in multiple sclerosis, including a favorable phase II study, but a decision was made by its pharmaceutical owner not to pursue FDA approval for multiple sclerosis, in part, because its patent expires in 2015. Instead, a biosimilar drug called ocrelizumab is in clinical development in phase III trials and is likely to be approved in 2016 or 2017.

Rituximab is widely considered highly effective in the treatment of multiple sclerosis by MS specialists across the country. Nearly 150 of these specialists have signed a petition urging insurers to cover the drug for MS. Its safety record has been demonstrated by more than 500,000 patient years of exposure in cancer and autoimmune diseases. It is a very reasonable option for MS patients who have failed or cannot tolerate existing 'on-label' FDA treatments for MS and its safety record is superior to some of these existing 'on-label' medications.

Several healthcare insurers, including some commercial insurers and government insurers, including Medicare and the state's Medicaid program will cover the cost of Rituximab treatment.

Rituximab costs approximately one half of all existing FDA 'on-label' treatments for MS.

Insurers that deny rituximab treatment for certain patients with multiple sclerosis cause those patients to be more disabled by their disease compared with their counterparts in whom this treatment is made available.

PRICE COMPARISONS FOR MULTIPLE SCLEROSIS MEDICATIONS
INFUSION THERAPIES*

Medication	Dose	Price per dose	Doses per year	Cost per year
Tysabri	300mg	$4,960	13	$64,480
Rituxan	1000mg	$7,244	4	$28,976
Lemtrada	12mg/day 1st year	$20,000	5	$98,000
	2nd year	$20,000	3	$60,000

INJECTABLE THERAPIES**

Medication	Dose	Price per dose	Doses per year	Cost per year
Avonex	30 mcg/vial	$1,145.85	52	$59,540
Avonex PEN	30 mcg/vial	$4,644.25	12	$55,731
Betaseron	.3 mg mcg/cc	$349.95	182	$63,691
Rebif	22 mcg/.5ml	$817.0	52	$42,484
	44 mcg/.5ml	$830.90	52	$43,160
Copaxone	20 mg/ml	$196.34	365	$71,664
Copaxone	40 mg/ml	$401.9	144	$57,744

ORAL THERAPIES**

Medication	Dose	Price per dose	Doses per year	Cost per year
Gilenya	.5 mg	$175.44	365	$64,035.6
Aubagio	DATA NOT AVAILABLE			
Tecfidera	DATA NOT AVAILABLE			

**source: CMS Weekly NADAC Reference File as of 02/04/2015

*source: Griffin Hospital In-Patient pharmacy

References

1. Abernethy A, et al. Systematic Review: Reliability of Compendia Methods for Off-Label Oncology Indications. Annals of Internal Medicine. 2009;150(5):336–343.

2. "Off-Label" and Investigational Use Of Marketed Drugs, Biologics, and Medical Devices - Information Sheet. (n.d.). Retrieved February 23, 2015, from http://www.fda.gov/RegulatoryInformation/Guidances/ucm126486.htm.

3. Prescription Drug Coverage. (n.d.). Retrieved February 23, 2015, from http://www.afscme.org/news/publications/health.-care/managed-care-what-you-dont-know-can-hurt-you/prescription-drug-coverage.